

# JOURNAL OF ANIMAL SCIENCE

*The Premier Journal and Leading Source of New Knowledge and Perspective in Animal Science*

## **Number of fetuses and conceptus growth throughout gestation in lines of pigs selected for ovulation rate or uterine capacity**

B. A. Freking, K. A. Leymaster, J. L. Vallet and R. K. Christenson

*J Anim Sci* 2007.85:2093-2103.

doi: 10.2527/jas.2006-766 originally published online May 15, 2007;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://jas.fass.org/cgi/content/full/85/9/2093>



**American Society of Animal Science**

[www.asas.org](http://www.asas.org)

# Number of fetuses and conceptus growth throughout gestation in lines of pigs selected for ovulation rate or uterine capacity<sup>1</sup>

B. A. Freking,<sup>2</sup> K. A. Leymaster, J. L. Vallet, and R. K. Christenson

USDA, ARS, US Meat Animal Research Center, Clay Center, NE 68933-0166

**ABSTRACT:** Selection for 11 generations in swine for ovulation rate (OR) or uterine capacity (UC) resulted in 19.6% greater prenatal survival at term in UC compared with OR. Our objective was to characterize the number of fetuses throughout gestation in each line, including an unselected control (CO) line. Five hundred ninety-three gilts produced over 4 farrowing seasons were subjected to unilateral-hysterectomy-ovariectomy at 160 d of age and mated within line at 280 d of age. Gilts were assigned within sire family to be slaughtered ( $\pm 2$  d) at d 25, 45, 65, 85, or 105 of gestation. Ovulation rate and number of live and dead fetuses were recorded for each pregnant gilt ( $n = 402$ ). Fetal and placental weights were also recorded. Ovulation rate of OR line gilts ( $18.0 \pm 0.3$  ova) exceeded ( $P < 0.001$ ) CO and UC lines ( $15.0 \pm 0.3$  and  $14.0 \pm 0.3$  ova, respectively). Line and gestational age interacted to affect number of live fetuses ( $P < 0.001$ ). Least squares means for CO were 10.1, 8.3, 7.2, 6.7, and 7.3 live fetuses for d 25, 45, 65, 85, and 105, respectively (average SE = 0.46 fetuses).

Corresponding means for OR were 13.4, 8.3, 7.9, 6.5, and 6.7 live fetuses, respectively (average SE = 0.44 fetuses). Means for UC were 10.2, 9.0, 8.5, 7.5, and 8.0 live fetuses, respectively (average SE = 0.47 fetuses). In each line, number of live fetuses at d 25 was approximately 72% of ovulation rate. Mortality to d 45 was greatest in OR, intermediate in CO, and least in UC. Reductions in live fetuses continued to occur from d 45 to 105, but line differences at d 45 were essentially maintained to d 105. Number of live fetuses in gilts at d 114 was estimated from each of the survival curves and predicted values of 7.0, 5.9, and 7.8 per uterine horn for CO, OR, and UC lines, respectively. Selection for uterine capacity improved fetal survival primarily during the time period between d 25 and 45. Relative growth rate coefficients throughout gestation for placental tissue indicated a change in rank of the line means, implicating a relative later growth pattern of placental tissue in the UC line.

**Key words:** fetal survival, placental growth, pig, uterine capacity

©2007 American Society of Animal Science. All rights reserved.

J. Anim. Sci. 2007. 85:2093–2103  
doi:10.2527/jas.2006-766

## INTRODUCTION

Prenatal and postnatal losses both limit opportunities for greater economic profitability of the swine industry. Evaluation of 11 generations of selection in pigs for increased ovulation rate (OR) or uterine capacity

(UC) was completed and preliminary analyses were reported (Leymaster and Christenson, 2000). Advantages in prenatal survival to term of the UC line compared with the OR line were large: 13.8% greater in intact gilts and 19.6% greater in unilateral hysterectomy-ovariectomy (UHO) gilts. Embryonic survival before d 25 of gestation (Youngs et al., 1994) and fetal survival from d 30 to parturition (Leymaster et al., 1986) have both been shown to contribute significantly to prenatal loss. In the UC line, however, it is unclear through what mechanism or specific time period(s) quantitative selection has improved prenatal survival.

Despite clear evidence of a genetic basis for litter size (Johnson et al., 1999), chromosomal regions containing QTL for the component traits of litter size have been difficult to detect (Rohrer et al., 1999; Cassady et al., 2001), indicating the genetic architecture is composed of many loci with small effects, which influence complex interactions. Gene expression data can provide complementary information to genomic scans for detection of

<sup>1</sup>Mention of trade names is necessary to report factually on available data; however, the USDA neither guarantees nor warrants the standard of the product, and the use of the same by USDA implies no approval of the product to the exclusion of others that may also be suitable. The authors acknowledge the expert technical assistance of T. Gramke for organizing data collection, J. Watts for secretarial support, the USMARC swine crew for expert animal husbandry and surgical assistance, and J. Schulte and the USMARC abattoir crew for assistance with data collection at slaughter. Helpful discussions with Harvey Freely on nonlinear functions were appreciated.

<sup>2</sup>Corresponding author: Brad.Freking@ars.usda.gov

Received November 21, 2006.

Accepted May 8, 2007.

the underlying genetic variation that influence messenger RNA profiles (Caetano et al., 2004; Blomberg et al., 2005). However, a better understanding of the temporal and spatial expression of line differences for embryo or fetal survival is needed to facilitate future gene discovery experiments within the OR and UC lines.

Our specific experimental objective was to characterize timing and magnitude of line differences in prenatal mortality in UHO gilts that were serially slaughtered at 25, 45, 65, 85, and 105 d of gestation. Additionally, the experiment generated data to characterize these selection lines for the proportionality of growth of fetal and placental components of developing conceptuses.

## MATERIALS AND METHODS

The experimental procedures were approved and performed in accordance with US Meat Animal Research Center Animal Care Guidelines and the Guide for Care and Use of Agricultural Animals in Agricultural Research and Teaching (FASS, 1999).

### *Experimental Design and Traits*

A 4-breed composite with equal contributions from Chester White, Landrace, Large White, and Yorkshire breeds was formed to estimate breed, heterosis, and recombination effects (Cassady et al., 2002). From a common base generation of this composite produced in 1986, selection was initiated during 1988 within 2 replicated seasons for ovulation rate estimated from laparoscopic examination of gilts in the OR line and increased uterine capacity of UHO surgically-altered gilts in the UC line, and an unselected control (CO) line was maintained. The selection experiment proceeded for 11 generations, and then all 3 lines were evaluated for responses in the component traits (Leymaster and Christenson, 2000). Relative to the unselected control, selection for ovulation rate increased ovulation rate by 3.2 ova, decreased uterine capacity by 0.97 pigs, decreased prenatal survival by 10.3%, and increased litter size by 0.30 pigs. Selection for uterine capacity increased ovulation rate by 0.13 ova, increased uterine capacity by 2.15 pigs, increased prenatal survival by 3.5%, and increased litter size by 0.62 pigs. Subsequent to this terminal evaluation, each line has been maintained under no intentional selection pressure, in 2 replicated seasons farrowing annually in March or September. Genetic diversity within each selection line and season was maintained by an intended target of 10 boars and 40 gilts farrowed.

Unilateral-hysterectomy-ovariectomy surgery was performed at approximately 160 d of age on 50 gilts of each line in each of 4 farrowing seasons, for a total of 593 gilts. Removal of the left or right uterine horn and ovary was done on an alternating basis. Justification and details of UHO as a procedure to estimate uterine capacity have been described previously (Christenson et al., 1987). All UHO-treated gilts that expressed es-

**Table 1.** Number of observations by selection line and stage of gestation

Selection line	Stage of gestation, d				
	25	45	65	85	105
Control	24	27	25	25	29
Ovulation rate	29	29	30	27	30
Uterine capacity	27	27	23	24	26

trus were single-sire mated at approximately 280 d of age to boars within the same selection line during a 21-d breeding season, avoiding paternal half-sib matings. A total of 502 gilts were mated and assigned to 1 of 5 gestational time points (d 25, 45, 65, 85, or 105) for slaughter. Gilts were assigned to a specific slaughter date to match one of the intended time points as closely as possible ( $\pm 2$  d) and also to distribute paternal half-sibs across as many of the 5 time points as possible.

Gilts were slaughtered at the US Meat Animal Research Center abattoir, where electrical stunning rendered them unconscious and they were exsanguinated. The reproductive tracts were removed and immediately evaluated. Tracts that displayed evidence of incomplete healing from UHO were discarded, whether or not the gilt was pregnant. The number of observations is presented by line and gestational stage (Table 1). Data collected from 402 gilts were analyzed. The ovary was excised and weighed before dissection and recorded for number of corpora lutea, representing ovulation rate. The cervix and broad ligament were closely trimmed, and gravid uterine weight was recorded. Length from the cervical end of the uterine body to the oviductal end of the uterine horn was recorded. Each tract was then opened along the antimesometrial border. Each fetus was removed by detachment from the umbilical cord, and status (alive, dead, or mummy) was recorded. Observation of a heartbeat was required for live status to be recorded. Weight of each fetus was also recorded. Placental tissue matching each fetus was separated from the endometrium and weighed. At 85 and 105 d of gestation, the tracts were allowed to sit at room temperature for 1 to 2 h after removal of the fetuses and before separation of the placental tissue. Traits calculated on a per gilt basis from individual fetal data included average and litter fetal and placental weights from live fetuses, total number of live fetuses, and total number of dead fetuses including mummified fetuses.

### *Statistical Analyses of Gilt Traits*

Data were analyzed with the mixed-model ANOVA procedure (SAS Inst. Inc., Cary, NC). Each trait described above was considered a trait of the gilt. Fixed effects of farrowing season (1, 2, 3, and 4), line (CO, OR, and UC), gestational age (25, 45, 65, 85, and 105 d), and 2-way interactions were fitted. The random effect of sire ( $n = 116$ ) of the gilt within farrowing season and line was used to test the line mean square. The Sat-

terthwaite option was used to approximate denominator degrees of freedom associated with the random effect of sire. To account for heterogeneous variances across gestational stages, data for fetal and placental weight were transformed by natural logarithm to remove a scaling effect (variances scaled proportional to the means).

Sampling issues when evaluating reproductive traits like litter size can generate least squares means that do not make sense from a biological point of view. For example, raw means and subsequently the least squares means estimated for number of live fetuses at d 105 were slightly greater than the estimates obtained at d 85 for each selection line. Obviously, litter size cannot increase from d 85 to 105, and this discrepancy was due to the random sample of gilts selected for each stage. A second statistical analysis was utilized to assess the dynamic relationship between ovulation rate and litter size (and thus prenatal survival) as a nonlinear decay function that can only decrease with time. To quantify prenatal survival curve characteristics, data for number of live fetuses were fitted to a nonlinear equation with 3 parameters:

$$f_{(d)} = A + (B \times e^{kd}), \quad [1]$$

where  $f_{(d)}$  = the number of live fetuses at a specific day of gestation,  $A$  = the asymptotic estimate of number live fetuses,  $B$  = the estimate of ovum wastage,  $k$  = the shape parameter of the curve, and  $d$  = the day of gestation. The nonlinear solution procedure (PROC NLIN) supported by SAS was used to provide estimates of the parameters using the Gauss-Newton method. All gilts provided data to estimate the number of potentially live fetuses at  $d = 0$  (based on the ovulation rate) and also 1 time point in gestation (25, 45, 65, 85, 105 d); thus, parameters were estimated from a data set with 2 observations per gilt. Parameters  $A$ ,  $B$ , and  $k$  were estimated for each line and also for data pooled across 2 or 3 lines. An  $F$ -ratio was calculated to test whether the estimation of the parameters specific to each line significantly improved the fit of the data relative to estimation of the parameters from pooled data sets. The test statistic calculated was as follows:

$$F = \frac{RSS_P - (\sum RSS_L) / Rdf_P - (\sum Rdf_L)}{\sum RSS_L / \sum Rdf_L},$$

where  $RSS$  represents the residual sums of squares,  $Rdf$  represents the residual degrees of freedom, and the subscripts  $P$  and  $L$  represent the pooled and contributing line-specific models, respectively. Comparison of a single equation pooling all 3 lines relative to 3 line-specific equations had 6 df in the numerator, whereas both 2-way comparisons of lines, each selection line (OR or UC) pooled with the CO, compared with contributing line-specific equations were 3-df tests. Large values of each  $F$ -statistic generated evidence that the pooled, sin-

gle model was inappropriate, and the relationships among ovulation rate and number of live fetuses differed between lines contributing to the pooled function.

A similar statistical approach was used to characterize and compare lines for average and total litter fetal and placental growth of live fetuses during gestation. A general exponential form of fetal growth was evaluated using the equation:

$$f_{(d)} = W \times e^{(X - Yd)d}, \quad [2]$$

where  $f_{(d)}$  = the weight of the live fetus or placental tissue at a specific day ( $d$ ) of gestation. Parameters estimated included an intercept  $W$  and 2 terms to describe the instantaneous growth rate  $X$  of the tissue (fetus or placenta) that decreased by the value  $Y$  each day of gestation. Parameters were again estimated for line-specific and combinations of pooled functions. An  $F$ -ratio (as described previously) was calculated to test whether estimation of the parameters specific to each line significantly improved fit of the data relative to estimation of parameters from pooled data sets. Large values of each  $F$ -statistic generated evidence that a pooled, single model was inappropriate and that the average or total fetal and placental growth rates differed between lines. As stated before for survival curves, comparison of a single equation for all lines relative to 3 line-specific equations was a 6-df test, whereas the 2 comparisons of the selection lines (OR and UC) each pooled with CO were 3-df tests.

### Statistical Analyses of Individual Conceptus Growth Traits

Allometric growth rate of fetal and placental components of conceptus tissue were evaluated using the equations and concepts for part-whole relationships developed by Huxley (1932). The allometric equation is represented in the following form:

$$Y = aX^b,$$

where  $Y$  = a measure of the component,  $X$  = a measure of the whole,  $a$  = a constant (value of  $Y$  when  $X = 1$ ), and  $b$  = the relative growth coefficient. This equation can be linearized to its logarithmic form,  $\ln(Y) = \ln(a) + b \cdot \ln(X)$ , to allow easily computed and interpreted solutions for the  $b$  parameter.

Conceptus tissue mass was calculated as the sum of fetal and placental weights ( $n = 3,371$  live conceptuses). Fixed effects of farrowing season (1, 2, 3, and 4), line (CO, OR, and UC), gestational age (25, 45, 65, 85, and 105 d), and 2-way interactions were fitted. Sire ( $n = 119$ ) of the fetus nested within farrowing season and line and also gilt ( $n = 402$ ) nested within sire of the fetus were fitted as random effects. The Kenward-Rogers option was used to approximate the denominator degrees of freedom associated with the random effects. Growth impetuses (relative growth rates) of the fetal



**Table 2.** Least-squares means (LSM) and residual SD (RSD) by stage of gestation

Item	Stage of gestation, d <sup>1</sup>									
	25		45		65		85		105	
	LSM	RSD	LSM	RSD	LSM	RSD	LSM	RSD	LSM	RSD
Ovulation rate	15.8	2.73	15.0	2.43	15.6	2.67	15.9	3.35	16.1	2.72
No. of live fetuses	11.2	3.29	8.5	2.15	7.9	2.27	7.0	1.95	7.3	1.96
No. of dead fetuses (dead + mummies)	0.9	1.23	1.6	1.43	1.0	1.03	1.4	1.50	1.2	1.22
Avg fetal wt, g	0.5	0.12	17.2	3.56	134.1	19.19	395.4	67.49	764.3	139.91
Litter fetal wt, g	5.3	1.92	145.3	45.78	1,051.2	308.97	2,684.9	722.23	5,444.7	1,282.83
Avg placenta wt, g	5.5	2.19	49.9	14.30	126.0	35.30	155.9	47.36	189.8	51.17
Litter placenta wt, g	58.0	23.33	418.6	143.42	980.6	383.32	1,053.3	366.24	1,364.1	419.15
Ovarian wt, g	12.3	2.19	13.8	2.42	15.3	2.97	16.1	3.69	17.7	5.75
Uterine length, cm	171.9	33.22	186.6	31.46	212.0	35.63	214.7	34.38	215.9	24.36

<sup>1</sup>There were 80, 83, 78, 76, and 85 observations at d 25, 45, 65, 85, and 105 of gestation, respectively.

and placental components of the conceptus were determined. Natural log-transformed values of the fetus or the placental weight were regressed on the natural log of the entire conceptus weight. A slope of 1.0 implies that the component tissue was growing at the same rate as the entire conceptus. A slope of less than 1.0 indicates the component tissue was growing at a slower rate than the entire conceptus, whereas a slope of greater than 1.0 indicates a faster rate of growth by the component tissue. Heterogeneity of these slopes throughout gestation and between selection lines was evaluated by fitting the subclass regressions within line and gestational age as well as within the interaction of line  $\times$  gestational age.

## RESULTS

### General

The UHO procedure was used to generate data that represent uterine capacity. Only 8 gilt observations (2% of all data) had an equivalent number of live fetuses at slaughter and ovulation rate, making determination of uterine capacity unknown. Four of those observations were from gilts slaughtered at d 25 when death loss associated with restrictions due to uterine capacity had yet to be expressed (Bennett and Leymaster, 1989). The remaining 4 observations were equivalent to, or exceeded, mean values for number of live fetuses within the respective line  $\times$  gestational age subclasses.

Effects of farrowing season, farrowing season  $\times$  gestational stage, and farrowing season  $\times$  line were not tabulated. Ovulation rate, and subsequently ovarian weight, was influenced by environmental effects associated with these farrowing seasons. Gilts born in September and mated during June had greater ovulation rates (1 ovum) than gilts born in March and mated during December. This seasonal influence on ovulation rate has been consistently observed within these lines (Ford et al., 2004).

### Characterization of Traits

Least-squares means and residual SD are presented by stage of gestation after accounting for selection line and farrowing season fixed effects (Table 2) to give an indication of the experimental variation. Inspection of the residual SD for average and litter fetal and placental weights provided justification for adjusting these raw data by log transformation to account for the scaling effect of the rapidly increasing means with increased stage of gestation.

### Line by Gestational Stage Interaction Means

Least-squares means, average SE, and levels of significance are presented for the line  $\times$  gestational stage interaction for traits measured on gilts (Table 3). This interaction was important ( $P < 0.05$ ) for number of live fetuses, number of dead fetuses, litter fetal weight, and uterine length; therefore, main effects were not summarized.

Ovulation rate was not influenced by interaction of line with gestational stage ( $P = 0.81$ ). Ovulation rate of OR line gilts ( $18 \pm 0.3$  ova) exceeded ( $P < 0.001$ ) both CO and UC lines ( $15.0 \pm 0.3$  and  $14.0 \pm 0.3$  ova, respectively). Ovarian weight increased during gestation and followed a similar pattern and ranking of lines as ovulation rate. Line interacted with gestational stage ( $P < 0.001$ ) to affect number of live fetuses and to establish the line-specific patterns of embryo survival. This interaction is the result of a change in rank of the lines during gestation. Line means for number of live fetuses to d 25 ranked the same as means for ovulation rate. Ranking of line means for number of live fetuses changed from d 25 to 45, with UC exceeding OR and CO despite being inversely ranked for ovulation rate. Subsequent to d 45, significant losses occurred in all 3 lines, yet the magnitude of line differences established for number of live fetuses at d 45 was essentially maintained to d 105. The significant line  $\times$  gestational age interaction for number of dead or mummified embryos was due to the greater than average number recovered

**Table 3.** Selection line  $\times$  gestational stage least-squares means, SE, and levels of significance for traits recorded at slaughter

Item <sup>1</sup>	Trait <sup>2</sup>								
	OR	OW, g	NLF	NDF	AFW, g	LFW, g	APW, g	LPW, g	UL, cm
CO $\times$ 25	15.1	12.0	10.1	0.4	0.5	4.1	5.4	49.0	178.4
OR $\times$ 25	18.1	13.0	13.4	1.2	0.4	5.9	3.9	52.1	165.5
UC $\times$ 25	14.2	11.9	10.2	1.1	0.5	4.7	5.9	57.4	172.8
Avg SEM <sup>3</sup>	0.54	0.7	0.45	0.25	NA	NA	NA	NA	6.2
CO $\times$ 45	14.3	13.0	8.3	1.4	17.1	134.0	49.0	381.8	186.6
OR $\times$ 45	17.1	15.4	8.3	2.4	17.0	136.0	42.5	340.7	178.4
UC $\times$ 45	13.4	13.0	9.0	1.1	16.5	145.6	53.2	469.7	194.9
Avg SEM	0.53	0.7	0.45	0.25	NA	NA	NA	NA	6.1
CO $\times$ 65	14.9	15.2	7.2	1.1	136.5	918.2	134.7	907.8	214.1
OR $\times$ 65	18.1	16.9	7.9	0.9	127.2	944.5	106.4	790.0	199.1
UC $\times$ 65	13.7	13.8	8.5	0.8	135.8	1,127.7	119.8	1,001.2	221.9
Avg SEM	0.56	0.7	0.47	0.26	NA	NA	NA	NA	6.4
CO $\times$ 85	15.7	15.4	6.7	1.4	422.7	2,751.5	169.0	1,107.6	224.0
OR $\times$ 85	17.8	17.8	6.5	1.4	347.9	2,119.2	113.5	688.8	189.0
UC $\times$ 85	14.4	15.1	7.5	1.3	391.5	2,709.2	153.7	1,065.3	225.6
Avg SEM	0.56	0.7	0.47	0.26	NA	NA	NA	NA	6.4
CO $\times$ 105	15.1	17.4	7.3	1.0	761.7	5,359.9	197.0	1,378.8	228.6
OR $\times$ 105	19.0	20.0	6.7	1.5	724.9	4,598.6	161.6	1,027.6	187.9
UC $\times$ 105	14.3	16.0	8.0	0.9	762.0	5,927.2	190.2	1,493.7	233.0
Avg SEM	0.53	0.7	0.44	0.24	NA	NA	NA	NA	6.1
Level of significance	0.81	0.7	0.001	0.04	0.23	0.001	0.17	0.09	0.02

<sup>1</sup>CO = control line; OR = ovulation rate line; UC = uterine capacity line; and the stage of gestation  $\pm$  2 d = 25, 45, 65, 85, 105.

<sup>2</sup>OR = ovulation rate, OW = ovarian weight; NLF = number live fetuses; NDF = number dead fetuses and mummies; AFW = average fetal weight; LFW = litter fetal weight; APW = average placental weight; LPW = litter placental weight, and UL = uterine length.

<sup>3</sup>Average SEM within gestational stage; NA = values are not applicable to traits that were log transformed before analyses. Least-squares means were back-transformed to the observed scale.

at d 45 in the OR line, compared with all other line  $\times$  stage combinations. The pattern of fetal losses was similar to the significant interaction of gestational age  $\times$  line for gravid uterine length. Greater fetal loss occurred in the OR line, and fetal growth did not distend the uterus beyond the length reached at d 65, in contrast to CO and UC, which continued to show increased length to d 105. As gestational age increased, the magnitude of differences between lines for litter fetal and placental weights increased, corresponding to line differences and ranking in number of live fetuses. Average fetal and placental weights were similar between CO and UC throughout gestation, and both began to exceed the OR line by d 85. This difference was increased at d 105.

### Line Effects on Fetal Survival

Estimates of parameters used to describe the number of live fetuses as a function of gestational age are presented in Table 4. Fetal losses occurred throughout gestation as measured by the nonlinear decay function described earlier (equation [1]). The asymptotic estimate of number of live fetuses per uterine horn, when ovulation rate is not limiting, is represented by parameter A: A is an estimate of uterine capacity with the caveat that gestation time is limited to 114 d. The B parameter is the estimated difference between the as-

ymptote and the value of the function at d = 0 (ovulation rate), and thus in biological terms represents total ovum wastage. Estimates of the k parameter dictate the shape of the decay pattern with gestational age. Three line-specific functions fit the data better than a single pooled function (Table 4; Figure 1). The *F*-tests also rejected ( $P < 0.01$ ) the null hypotheses that OR and CO were equivalent, as well as UC and CO. Analysis of residual values did not reveal any bias associated with the line-specific equations. In general, the curve for OR differed from the other 2 lines by having the greatest value of B (ovum wastage), and the lowest value of A. The curve for UC exhibited the lowest value of B and the greatest value of A. Numbers of live fetuses at d 114 were predicted for each line with values of 7.0, 5.9, and 7.8 live pigs per uterine horn for CO, OR, and UC, respectively. When expressed as deviations from CO, these results imply that single trait selection for uterine capacity increased the intended trait by 0.8 pigs per uterine horn, and single trait selection for ovulation rate decreased uterine capacity by 1.1 pigs per uterine horn. These results would support a negative genetic correlation between ovulation rate and uterine capacity.

### Line Effects on Fetal and Placental Growth Curves

Parameters were estimated to describe average and litter fetal and placental weights as a function of gesta-

**Table 4.** Estimates of parameters and statistics describing number of live fetuses as a nonlinear function of gestational age

Selection line(s) included in the equation	Parameter <sup>1</sup>			Residual		
	A ± SE	B ± SE	K ± SE	Sums of squares	df	F <sup>2</sup>
Line-specific equations						
Control (CO)	6.88 ± 0.43	8.21 ± 0.47	-0.040 ± 0.008	1,714	257	—
Ovulation rate (OR)	5.02 ± 0.82	13.06 ± 0.83	-0.024 ± 0.004	2,192	287	—
Uterine capacity (UC)	7.65 ± 0.50	6.39 ± 0.54	-0.035 ± 0.009	1,693	251	—
Pooled equations						
CO + OR	6.02 ± 0.48	10.64 ± 0.49	-0.029 ± 0.004	4,626	547	33.4**
CO + UC	7.25 ± 0.33	7.32 ± 0.36	-0.038 ± 0.006	3,513	511	5.3**
CO + OR + UC	6.53 ± 0.38	9.30 ± 0.40	-0.030 ± 0.004	6,986	801	32.8**

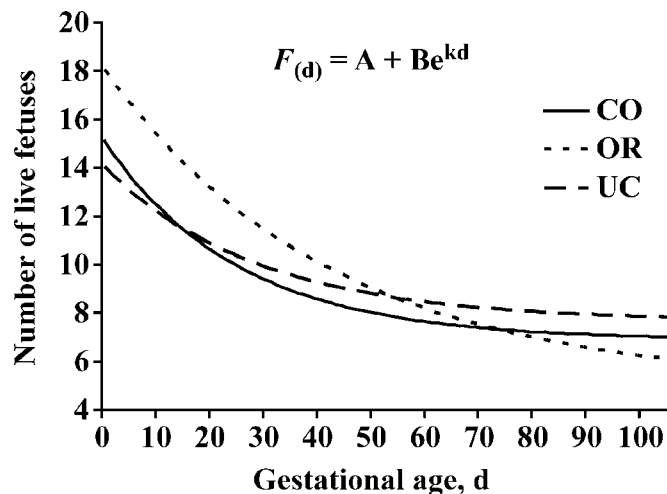
<sup>1</sup>Function: number of live fetuses =  $f(d) = A + Be^{kd}$ , where A = asymptotic estimate of fetuses per uterine horn, B = ovum wastage, k = curve shape parameter, and d = days of gestation with a limit to the range of day from 0 to 114.

<sup>2</sup>F-ratio tests the hypothesis that the contributing line-specific functions are equivalent. Numerator df are 6 for the 3-line pooled equation and 3 for the equations pooling 2 lines.

\*\*Contributing line-specific functions differed from the pooled function,  $P < 0.01$ .

tional age (Table 5). A general exponential form of fetal growth was evaluated using equation [2] as previously described. The null hypothesis of a single pooled function to describe average fetal weight was rejected ( $P < 0.01$ ). The 2-line pooled functions indicated no evidence to separate CO and UC from each other, but rejected ( $P < 0.01$ ) the hypothesis that CO and OR functions were similar. The OR-specific function indicated a slower growth rate for the average fetus in an OR gilt during the interval between d 65 and 85 of gestation, and this resulting weight difference remained at d 105 (Figure 2).

For litter fetal weight, 3 line-specific functions fitted the data better than a single pooled function ( $P < 0.01$ ).



**Figure 1.** Line-specific functions for number of live fetuses from ovulation to 105 d of gestation. CO = control line; OR = ovulation rate line; and UC = uterine capacity line.  $f(d)$  = the number of live fetuses at a specific day of gestation, A = the asymptotic estimate of number live fetuses, B = the estimate of ovum wastage, k = the shape parameter of the curve, and d = the day of gestation.

The F-tests also indicated a rejection ( $P < 0.05$ ) of null hypotheses that either of the selected (OR and UC) lines were equal to the CO line. As gestational age increased, UC gilts had more fetuses at similar average weights, thus greater litter fetal weight, compared with CO gilts. Gilts from the OR line had fewer fetuses during the latter stages of gestation and had fetuses with lower average weights throughout gestation than CO gilts.

Analysis of average placental weight (Figure 3) rejected ( $P < 0.01$ ) the hypothesis that all lines were similar. The F-tests indicated that UC and CO were similar to each other and that functions for CO and OR were different ( $P < 0.01$ ). This difference was evident by d 45, and the magnitude increased until d 85 when all 3 lines reached a plateau phase of placental growth.

The null hypothesis of a single pooled function for litter placental weight ( $P < 0.01$ ) was rejected as were null hypotheses that OR or UC were equal to CO ( $P < 0.01$ ). Similar to line effects on litter fetal weight, litter placental weight was greatest for UC, followed by CO, then OR. Divergence of OR from CO was already detectable near d 45 of gestation, despite a similar number of fetuses at that stage. The UC difference from CO was primarily due to differences in number of fetuses at d 85 and 105 because average placental weights were similar.

#### Relative Growth Rates of Fetal and Placental Tissues

Results from tests of homogeneity of growth coefficients among selection lines and gestational stages relating fetal and placental growth relative to the entire conceptus are presented in Table 6. Differences ( $P < 0.05$ ) were detected among combinations of lines and gestational stages for relative growth of the placenta and approached statistical significance ( $P < 0.10$ ) for relative growth of the fetus. Based on these results, estimates of relative growth coefficients for the interac-

**Table 5.** Estimates of parameters<sup>1</sup> describing fetal and placental growth as a nonlinear function of gestational age

Item	Pooled equations <sup>2,3</sup>			Line-specific equations		
	CO + OR + UC	CO + OR	CO + UC	CO	OR	UC
Avg fetal wt, parameter						
W ± SE	0.141 ± 0.098	0.143 ± 0.120	0.089 ± 0.078	0.057 ± 0.072	0.349 ± 0.369	0.139 ± 0.171
X ± SE	0.142 ± 0.015	0.142 ± 0.119	0.155 ± 0.020	0.167 ± 0.028	0.117 ± 0.024	0.143 ± 0.027
Y ± SE	0.0006 ± 0.00008	0.0006 ± 0.0001	0.0006 ± 0.0001	0.0007 ± 0.0002	0.0004 ± 0.0001	0.0006 ± 0.0001
F-test	4.15**	5.54**	0.83	—	—	—
Litter fetal wt, parameter						
W ± SE	3.142 ± 2.706	3.106 ± 3.320	1.733 ± 1.655	0.793 ± 1.092	9.473 ± 13.998	3.431 ± 4.392
X ± SE	0.115 ± 0.019	0.115 ± 0.024	0.131 ± 0.021	0.149 ± 0.031	0.085 ± 0.033	0.115 ± 0.029
Y ± SE	0.0004 ± 0.0001	0.0004 ± 0.0001	0.0005 ± 0.0001	0.0006 ± 0.0002	0.0002 ± 0.0002	0.0004 ± 0.0002
F-test	9.93**	7.92**	3.65*	—	—	—
Avg placental wt, parameter						
W ± SE	3.195 ± 0.993	3.103 ± 1.273	2.768 ± 1.052	2.270 ± 1.383	4.216 ± 1.955	3.431 ± 4.392
X ± SE	0.080 ± 0.008	0.081 ± 0.010	0.086 ± 0.010	0.093 ± 0.015	0.068 ± 0.012	0.115 ± 0.029
Y ± SE	0.0004 ± 0.00005	0.0004 ± 0.0006	0.0004 ± 0.00006	0.0005 ± 0.00009	0.0003 ± 0.00007	0.0004 ± 0.00007
F-test	7.65**	13.33**	1.82	—	—	—
Litter placental wt, parameter						
W ± SE	38.472 ± 12.331	37.996 ± 15.154	33.282 ± 11.792	27.437 ± 13.687	49.678 ± 28.193	39.587 ± 19.871
X ± SE	0.068 ± 0.008	0.067 ± 0.010	0.074 ± 0.0009	0.079 ± 0.013	0.058 ± 0.015	0.070 ± 0.013
Y ± SE	0.0003 ± 0.00005	0.0003 ± 0.00006	0.0004 ± 0.00006	0.0004 ± 0.00008	0.0003 ± 0.00009	0.0003 ± 0.00008
F-test	14.57**	10.68**	7.96**	—	—	—

<sup>1</sup>Fetal or placental weight =  $f(d) = W \times e^{(X-Yd)}$ , where W, X, Y represent curve parameters and d represents days of gestation with a limit to the range of d from 0 to 114.

<sup>2</sup>F-ratio tests the hypothesis that the contributing line-specific functions are equivalent. Numerator df are 6 for the 3-line pooled equation and 3 df for the equations pooling 2 lines.

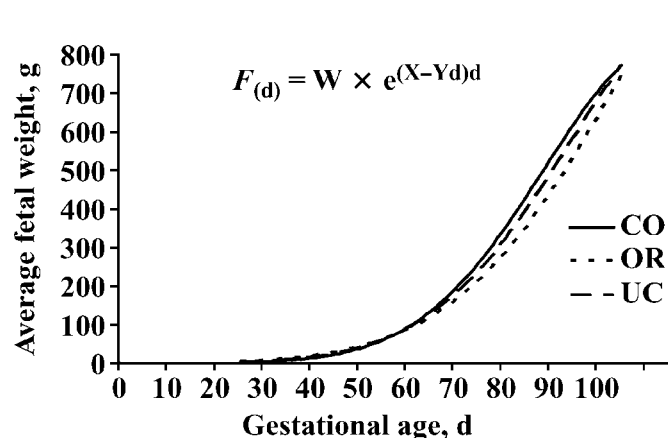
<sup>3</sup>CO = control line; OR = ovulation rate line; and UC = uterine capacity line.

\* $P < 0.05$ ; and \*\* $P < 0.01$ .

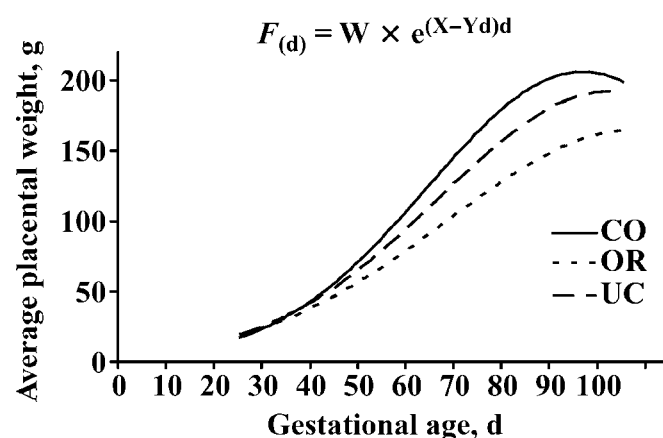
tion of selection line with gestational stage are presented in Table 7.

Relative growth rate coefficients for fetal weight as a component of the conceptus were less than 1.0 during the early stages of gestation and approached 1.0 near term. Rejection of the hypothesis of common relative fetal growth coefficients ( $P < 0.10$ ) for the interaction

of line and gestational stage was due primarily to a small coefficient in the CO line at d 25 and a large growth coefficient in the OR line at d 65. In contrast to what was observed for fetal weight, relative growth rate coefficients for placental weight as a component of the conceptus increased from 1.1 to nearly 1.4 at d 65 and



**Figure 2.** Line-specific growth curves for average fetal weight. CO = control line; OR = ovulation rate line; and UC = uterine capacity line.  $f(d)$  = the weight of the live fetus or placental tissue at a specific day (d) of gestation. Parameters estimated included an intercept W and 2 terms to describe the instantaneous growth rate X of the tissue (fetus or placenta) that decreased by the value Y each day of gestation.



**Figure 3.** Line-specific growth curves for average placental weight. CO = control line; OR = ovulation rate line; and UC = uterine capacity line.  $f(d)$  = the weight of the live fetus or placental tissue at a specific day (d) of gestation. Parameters estimated included an intercept W and 2 terms to describe the instantaneous growth rate X of the tissue (fetus or placenta) that decreased by the value Y each day of gestation.



**Table 6.** Tests of homogeneity of slopes among selection lines and gestational stages for regression of natural logarithm of fetal or placental weight on natural logarithm of conceptus weight

Dependent variable and effect	Numerator df	F-value
ln (fetal wt)		
ln (conceptus wt)	1	6,249.4***
ln (conceptus wt) × line	2	1.5
ln (conceptus wt) × gestational stage	4	425.2***
ln (conceptus wt) × line × gestational stage	8	1.9†
ln (placental wt)		
ln (conceptus wt)	1	39,126.5***
ln (conceptus wt) × line	2	0.3
ln (conceptus wt) × gestational stage	4	123.4***
ln (conceptus wt) × line × gestational stage	8	2.0*

† $P < 0.10$ , \* $P < 0.05$ , and \*\*\* $P < 0.001$ .

subsequently decreased to near 1.0 at d 105. The significant interaction was primarily the result of UC changing rank throughout gestation relative to OR and CO. At stages before d 65 and at d 85, the relative growth coefficients were numerically the lowest for UC. However, at d 65 and 105, UC coefficients were greatest, perhaps indicating the relative later growth of placental tissue in this line.

## DISCUSSION

This is the largest reported experiment to examine prenatal survival throughout gestation in pigs. The primary objective was to characterize how selection line and gestational stage interacted to affect prenatal survival and litter size when ovulation rate was not a limiting component. Before this experiment, only Knight et al. (1977) reported on survival of fetuses throughout the entire range of gestation on UHO altered gilts. These authors proposed that insufficient placental de-

velopment between d 20 and 30 of gestation had a significant influence on subsequent fetal growth and survival in a crowded uterine environment. Placental development and subsequent fetal survival and growth were shown to be significantly correlated. Johnson et al. (1999) provided strong evidence of a genetic component to embryonic survival ( $h^2 = 0.14$ ) and a positive genetic correlation with litter size ( $r_g = 0.36$ ) using a selection index optimally weighted for ovulation rate and embryo survival to d 50 of gestation. Detrimental correlated responses to selection for that index were increased stillborns and mummified fetuses (died after d 50) as well as decreased number weaned, which was attributed to decreased birth weights of pigs born alive.

Lines of pigs that differed greatly in conceptus survival were created (Leymaster and Christenson, 2000) by selection for ovulation rate or uterine capacity, the number of fetuses carried to term in UHO-treated gilts. The intent was not to select for litter size directly, but rather to select independently for the component traits and provide data to validate a litter size model (Bennett and Leymaster, 1989). The OR line had no intended selection pressure for uterine capacity, and similarly no selection pressure for ovulation rate was intended in the UC line. Early embryo survival before d 25 of gestation (Youngs et al., 1994) and uterine capacity effects from d 30 to parturition (Leymaster et al., 1986; Johnson et al., 1999) have both been shown to contribute significantly to prenatal losses. It was not known when increased uterine capacity provided a more favorable uterine environment to increase survival rates. Selection in the UC line was based on number born at farrowing, allowing for expression of accumulated effects throughout gestation. The current experiment was specifically designed to address the timing of prenatal mortality in these unique lines. Line differences in timing of prenatal mortality have implications on approaches to investigate genetic variation underlying the loci affected by selection. Physiological and metabolic pathway targets considered for evaluation may differ depending on timing of mortality.

**Table 7.** Selection line and gestational stage-specific estimates of relative growth coefficients of fetal and placental components relative to total conceptus weight

Selection line	Gestational stage, d	Fetal wt coefficient <sup>1</sup> ± SE	Placental wt coefficient <sup>1</sup> ± SE
Control	25	0.167 ± 0.021	1.104 ± 0.016
	45	0.355 ± 0.026	1.293 ± 0.020
	65	0.664 ± 0.035	1.381 ± 0.027
	85	0.912 ± 0.038	1.262 ± 0.029
	105	1.011 ± 0.036	0.978 ± 0.027
Ovulation rate	25	0.276 ± 0.014	1.106 ± 0.011
	45	0.365 ± 0.029	1.292 ± 0.021
	65	0.726 ± 0.028	1.370 ± 0.021
	85	0.916 ± 0.033	1.268 ± 0.025
	105	0.992 ± 0.036	1.035 ± 0.027
Uterine capacity	25	0.289 ± 0.019	1.079 ± 0.014
	45	0.344 ± 0.032	1.247 ± 0.024
	65	0.672 ± 0.035	1.421 ± 0.027
	85	0.927 ± 0.038	1.205 ± 0.029
	105	0.982 ± 0.037	1.078 ± 0.028

<sup>1</sup>Coefficient is relative to total conceptus weight.

Downloaded from [jas.fass.org](http://jas.fass.org) at USDA Natl Agricultural Library on August 20, 2008.

Copyright © 2007 American Society of Animal Science. All rights reserved. For personal use only. No other uses without permission.

Differences between lines in ovulation rate were similar to those estimated in the terminal evaluation of the selection phase (Leymaster and Christenson, 2000), with OR exceeding the other 2 lines by 3 to 4 ova. Similar rates of embryonic loss to d 25 for all 3 lines indicate that losses due to reduced ovum quality or maturation, fertilization failures, and genetic abnormalities were not affected by OR selection. Also, direct selection for uterine capacity did not result in a significant increase of live embryos before d 25. Numbers of dead embryos observed at this early stage accounted for less than 30% of the ova lost to that point. If there is a genetic basis for potential embryo viability as defined in Bennett and Leymaster (1989), associated with selection for ovulation rate or uterine capacity, it was not evident in this study. Least-squares means for ovulation rate and number of live fetuses indicated 67, 74, and 72% survival to d 25 for CO, OR, and UC lines, respectively. These estimates of embryonic viability at this time point were slightly lower than the modeled value of 0.82 estimated from a summary of literature at that time (Bennett and Leymaster, 1990).

Dramatic changes between lines in fetal losses between d 25 and 45 were evident (Figure 1) and provided the majority of the differences between lines. Gilts from the OR line had less endometrial space available per embryo at implantation and this severely crowded environment resulted in lower average placental weights and greater fetal losses during the critical period for placental development. Compared with the CO line, the UC line had a similar initial density of embryos per unit of endometrial space, yet provided a superior uterine environment to increase number of live fetuses and maintain similar average fetal and placental weights. A greater number of UC embryos developed a sufficient placenta and survived to and beyond d 45, producing greater litter placental and fetal weights. Despite the smallest number of live fetuses, the OR line had the lowest average fetal and placental weights. Apparently, the OR line was not able to capitalize on uterine space associated with early-stage embryos that died, suggesting that the space allotted to each placenta is fixed during early gestation. This conclusion is consistent with a report by Lamberson and Eckardt (1996) that also indicated surviving fetuses do not make use of uterine space vacated by nonsurviving littermates.

The period of rapid embryo elongation and communication among potential littermates to allocate available uterine space and the subsequent initiation of attachment occurs by d 13, with complete attachment over the entire surface of the conceptus by d 26 (Foxcroft et al., 2000). A rapid increase of allantoic fluid occurs between d 20 and 30 that is associated with expansion of the chorio-allantoic membranes and direct intimate contact between the placenta and endometrial surface (Knight et al., 1977). Development of the placental membrane length during this period is critical to the overall allocation of endometrial space occupied by an individual embryo. Placental length increases rapidly

from d 20 to 30 and then continues to increase at a slower rate to d 60 when it reaches a plateau, with placental weight reaching a plateau approximately 10 d later (Pomeroy, 1960; Knight et al., 1977). This rapid placental growth period requires a high level of coordination for appropriate amino acid metabolism to optimize the DNA and protein synthesis machinery to support this level of cell proliferation. During this specific time of gestation (from d 20 to 40), placental branched chain amino acid transport, transamination, and activities of related enzymes increase markedly (Self et al., 2004). It has been demonstrated that d 40 of gestation is also coincident with maximum placental glutamine synthesis and when glutamine is most abundant in fetal allantoic fluid (Self et al., 2004). Uptake of glutamine by the embryo becomes critical in its role as a substrate for fetal synthesis of arginine because uterine uptake of arginine is not sufficient to support fetal growth during late pregnancy (Wu et al., 1999). Pathways and enzymes associated with amino acid metabolism changes in this critical time period would make reasonable candidate genes for intensive evaluation of altered allele frequencies and functional analysis in these selected lines.

Development of fetal erythropoiesis also coincides with the critical interval from d 20 to 40. It has been suggested that intrauterine crowding results in impaired fetal erythropoiesis (Pearson et al., 1998) and breed differences exist in the rate of blood cell development (Vallet et al., 2003). Allelic variation at the erythropoietin receptor gene (EPOR) was discovered in 2 populations and the fetal genotype was associated with a functional increase in the expression of the EPOR gene and improved fetal survival (Vallet et al., 2005; Vallet and Freking, 2006). Although this functional polymorphism was encountered within the 3 selection lines from the current experiment, the frequency of the favorable allele was very low (less than 5%) and only marginally greater in the UC line. In spite of a rather strong indication of this single locus affecting embryo survival and litter size (Vallet et al., 2005), the frequency of this polymorphism was not increased by direct selection for uterine capacity. This evidence is consistent with the concept that genetic architecture of uterine capacity is polygenic with many loci each contributing small effects on the phenotype.

After the critical d 25 to 45 interval, line differences in average placental weights became evident (decreased OR placental weights at d 45) and preceded differences in fetal weights between d 65 and 85. This result is consistent with concepts of maximum placental growth occurring earlier than fetal growth (Pomeroy, 1960) and that restriction of placental growth leads to a subsequent restriction of fetal growth. At what point restriction of placental growth becomes a critical factor is not clear. Conceptus estrogen production may play a critical role in promoting growth of the conceptus trophoblast by stimulating endometrial production of growth factors (Wilson and Ford, 2000; Jaeger et al., 2001;

Blomberg et al., 2006). Variation in mitotic activity of trophoctoderm between and among conceptuses may play a critical role in determining ultimate placental development and function among embryos competing for limited maternal resources. Changes in embryonic estrogen secretion or production in these lines have been investigated with mRNA from d 11 to 12, and preliminary reports indicate decreased levels of steroidogenic transcripts by the OR line (Miles et al., 2006). However, it is not yet clear whether this is a cause of reduced elongation in the OR line or a consequence of increased intrauterine crowding experienced by these blastocysts. It seems reasonable that greater synchrony of early embryo development can lead to more uniform placental development and fewer embryos at risk for loss. However, typical embryonic growth can also occur up to approximately d 30 in the pig even in the absence of a functional placenta, as in the case of gynogenetic embryos (Surani et al., 1990; J. Piedrahita, North Carolina State University, Raleigh, NC, personal communication). Vallet et al. (2002) reported that small conceptus diameter on d 11 was not correlated with uterine capacity or with placental weights during later stages of pregnancy. Fetal growth, in terms of mass, typically begins to exceed placental growth by d 70 (Pomeroy, 1960). This is supported by our analysis of data for relative growth coefficients (Table 7). Relative growth coefficients were greater for placental tissue compared with fetal tissue to d 65 and then decreased to a similar rate as that of fetal tissues near term. Relative growth coefficients for the UC line (Table 7) indicated a later maturing placental tissue, and it appears that the steepest portion of the growth curve (Figure 3) for placenta coincides with greatest relative growth coefficients.

Wilson et al. (1999) hypothesized that the increased ratio of fetal mass to placental mass could be used as a criterion to increase litter size based on observations of greater ratios in Meishan pigs compared with occidental breeds and a single generation of divergent selection yielding differences in litter size. This concept was further examined in a line of pigs selected for components of litter size, and results indicated that uterine capacity increases in the selected line were achieved through a different mechanism than altering the ratio of fetal weight to placental weight, as the control line exceeded the selected line for this ratio (Mesa et al., 2003). Similar to Mesa et al. (2003), changes in uterine capacity from the current experiment were not achieved through altered placental efficiency measured as fetal weight relative to placental weight. Functions for number of live fetuses were significantly different between UC and CO (Table 4), but UC and CO differences were not detected for either average fetal weight (Table 5) or average placental weight (Table 6). It is likely that placental function rather than weight is most critical to support fetal development. Divergent selection for 4 generations for this ratio generated little evidence to suggest that selection for improved placental efficiency

would increase litter size (Mesa et al., 2005). All of these studies are based on the concept that placental and fetal mass components at term are predictive of litter size, when in reality it is likely that the critical time period in terms of placental support of larger litters occurs much earlier in gestation. In the current experiment, the UC line had greater relative growth coefficients for the placenta at d 65 and 105, and litter size differences were established by d 45.

Anecdotal observations while separating placental and uterine tissues suggested that placental tissue from the UC line was physically stronger and could withstand greater pressure before tearing. Perhaps altered collagen or other structural proteins were the result of direct selection for uterine capacity, improving the function of individual placenta to support fetal growth under restricted conditions. Understanding improved placental function is critically important because ovulation rate has increased within swine industry populations and a concomitant increase in uterine capacity must also occur to maximize the opportunities in litter size. Even if the value for litter size has approached the industry optimum, postnatal survival is a problem. The importance of prenatal programming to postnatal performance has been documented (Foxcroft et al., 2006). The current experiment is the largest one to report values for number of live fetuses throughout the gestation interval and has shed light on the temporal expression of line differences for fetal survival. Results indicated the importance of placental tissues in expression of these differences. Our intention is to pursue placental transcriptome differences that resulted from selection for components of litter size and resulted in line differences for fetal survival.

Increased ovulation rates have resulted in less than optimal piglet survival rates during prenatal and early postnatal periods and have hindered the desired outcome of increased numbers of pigs weaned. Understanding the biological basis for improved uterine capacity as a consequence of genetic selection would allow exploitation of greater levels of reproductive potential. Unique fetal survival curves resulted from selection of pigs for ovulation rate or uterine capacity. Embryonic losses from ovulation to d 25 were proportional to ova shed in all 3 lines. Direct selection for uterine capacity has increased survival of fetuses to term, primarily by increasing survival between d 25 and 45 of gestation without altering fetal or placental weights. Losses continued to occur from d 45 to 105, but line differences in number of fetuses at d 45 were essentially maintained to d 105. The critical period of time identified coincides with rapid development of the placenta and focuses attention on metabolic pathways that can create and develop a placental environment capable of maintaining more fetuses of a similar birth weight to term.

## LITERATURE CITED

- Bennett, G. L., and K. A. Leymaster. 1989. Integration of ovulation rate, potential embryonic viability and uterine capacity into a model of litter size in swine. *J. Anim. Sci.* 67:1230–1241.



- Bennett, G. L., and K. A. Leymaster. 1990. Genetic implications of a simulation model of litter size in swine based on ovulation rate, potential embryonic viability and uterine capacity: I. Genetic theory. *J. Anim. Sci.* 68:969–979.
- Blomberg, L. A., W. M. Garrett, M. Guillomot, J. R. Miles, T. S. Sonstegard, C. P. Van Tassell, and K. A. Zuelke. 2006. Transcriptome profiling of the tubular porcine conceptus identifies the differential regulation of growth and developmentally associated genes. *Mol. Reprod. Dev.* 73:1491–1502.
- Blomberg, L. A., E. L. Long, T. S. Sonstegard, C. P. Van Tassell, J. R. Dobrinsky, and K. A. Zuelke. 2005. Serial analysis of gene expression during elongation of the peri-implantation porcine trophoctoderm (conceptus). *Physiol. Genomics* 20:188–194.
- Caetano, A. R., R. K. Johnson, J. J. Ford, and D. Pomp. 2004. Microarray profiling for differential gene expression in ovaries and ovarian follicles of pigs selected for increased ovulation rate. *Genetics* 168:1529–1537.
- Cassady, J. P., R. K. Johnson, D. Pomp, G. A. Rohrer, L. D. Van Vleck, E. K. Spiegel, and K. M. Gilson. 2001. Identification of quantitative trait loci affecting reproduction in pigs. *J. Anim. Sci.* 79:623–633.
- Cassady, J. P., L. D. Young, and K. A. Leymaster. 2002. Heterosis and recombination effects on pig growth and carcass traits. *J. Anim. Sci.* 80:2286–2302.
- Christenson, R. K., K. A. Leymaster, and L. D. Young. 1987. Justification of unilateral hysterectomy ovariectomy as a model to evaluate uterine capacity in swine. *J. Anim. Sci.* 65:738–744.
- FASS. 1999. Guide for Care and Use of Agricultural Animals in Agricultural Research and Teaching. 1st ed. Fed. Anim. Sci. Soc., Savoy, IL.
- Ford, J. J., T. H. Wise, and R. K. Christenson. 2004. Lack of an association between plasma follicle-stimulating hormone concentrations and ovarian weight in prepubertal gilts. *J. Anim. Sci.* 82:472–478.
- Foxcroft, G. R., W. T. Dixon, S. Novak, C. T. Putman, S. C. Town, and M. D. Vinsky. 2006. The biological basis for prenatal programming of postnatal performance in pigs. *J. Anim. Sci.* 84(Suppl.):E105–E112.
- Foxcroft, G. R., W. T. Dixon, B. K. Treacy, L. Jiang, S. Novak, J. Mao, and F. C. L. Almeida. 2000. Insights into conceptus-reproductive tract interactions in the pig. *Proc. Am. Soc. Anim. Sci.*, 1999. <http://www.asas.org/jas/symposia/proceedings/0919.pdf> Accessed May 23, 2006.
- Huxley, J. S. 1932. Problems of relative growth. Meuen and Co., London, UK.
- Jaeger, L. A., G. A. Johnson, H. Ka, G. Garlow, R. C. Burghardt, T. E. Spencer, and F. W. Bazer. 2001. Functional analysis of autocrine and paracrine signaling at the uterine-conceptus interface in pigs. *Reprod. Suppl.* 58:191–207.
- Johnson, R. K., M. K. Nielsen, and D. S. Casey. 1999. Responses in ovulation rate, embryonal survival, and litter traits in swine to 14 generations of selection to increase litter size. *J. Anim. Sci.* 77:541–557.
- Knight, J. W., F. W. Bazer, W. W. Thatcher, D. E. Franke, and H. D. Wallace. 1977. Conceptus development in intact and unilaterally hysterectomized-ovariectomized gilts: Interrelations among hormonal status, placental development, fetal fluids and fetal growth. *J. Anim. Sci.* 44:620–637.
- Lamberson, W. R., and G. R. Eckardt. 1996. Local changes in uterine dimensions in the pregnant pig. *Anim. Reprod. Sci.* 43:35–41.
- Leymaster, K. A., and R. K. Christenson. 2000. Direct and correlated responses to selection for ovulation rate or uterine capacity in swine. *J. Anim. Sci.* 78(Suppl. 1):68. (Abstr.)
- Leymaster, K. A., R. K. Christenson, and L. D. Young. 1986. A biological model to measure uterine potential for litter size in swine. *Proc. 3rd World Congr. Genet. Appl. Livest. Prod.*, Lincoln, NE. XI:209–214.
- Mesa, H., T. J. Safranski, K. A. Fischer, K. M. Cammack, and W. R. Lamberson. 2005. Selection for placental efficiency in swine: Genetic parameters and trends. *J. Anim. Sci.* 83:983–991.
- Mesa, H., T. J. Safranski, R. K. Johnson, and W. R. Lamberson. 2003. Correlated response in placental efficiency in swine selected for an index of components of litter size. *J. Anim. Sci.* 81:74–79.
- Miles, J. R., L. A. Blomberg, B. A. Freking, and K. A. Zuelke. 2006. Lines of pigs selected for component traits of litter size exhibit differential gene regulation at the onset of embryo (trophoctoderm) elongation. Page 18 in *Proc. 32nd Int. Conf. IETS*, Orlando, FL. (Abstr.)
- Pearson, P. L., H. G. Klemke, R. K. Christenson, and J. L. Vallet. 1998. Uterine environment and breed effects on erythropoiesis and liver protein secretion in late embryonic and early fetal swine. *Biol. Reprod.* 58:911–918.
- Pomeroy, R. W. 1960. Infertility and neonatal mortality in the sow: III. Neonatal mortality and foetal development. *J. Agr. Sci.* 54:31–56.
- Rohrer, G. A., J. J. Ford, T. H. Wise, J. L. Vallet, and R. K. Christenson. 1999. Identification of quantitative trait loci affecting female reproduction traits in a multigeneration Meishan-White composite swine population. *J. Anim. Sci.* 77:1385–1391.
- Self, J. T., T. E. Spencer, G. A. Johnson, J. Hu, F. W. Bazer, and G. Wu. 2004. Glutamine synthesis in the developing porcine placenta. *Biol. Reprod.* 70:1444–1451.
- Surani, M. A., R. Kothary, N. D. Allen, P. B. Singh, R. Fundele, A. C. Ferguson-Smith, and S. C. Barton. 1990. Genome imprinting and development in the mouse. *Dev. Suppl.* 89–98.
- Vallet, J. L., and B. A. Freking. 2006. An erythropoietin receptor (EPOR) gene polymorphism (SNP) alters EPOR mRNA in fetal liver of swine during early gestation. *J. Anim. Sci.* 84(Suppl. 1):450. (Abstr.)
- Vallet, J. L., B. A. Freking, K. A. Leymaster, and R. K. Christenson. 2005. Allelic variation in the erythropoietin receptor gene is associated with uterine capacity and litter size in swine. *Anim. Genet.* 36:97–103.
- Vallet, J. L., H. G. Klemke, and R. K. Christenson. 2002. Interrelationships among conceptus size, uterine protein secretion, fetal erythropoiesis, and uterine capacity. *J. Anim. Sci.* 80:729–737.
- Vallet, J. L., H. G. Klemke, R. K. Christenson, and P. L. Pearson. 2003. The effect of breed and intrauterine crowding on fetal erythropoiesis on day 35 of gestation in swine. *J. Anim. Sci.* 81:2352–2356.
- Wilson, M. E., N. J. Biensen, and S. P. Ford. 1999. Novel insights into the control of litter size in pigs, using placental efficiency as a selection tool. *J. Anim. Sci.* 77:1654–1658.
- Wilson, M. E., and S. P. Ford. 2000. Effect of estradiol-17 beta administration during the time of conceptus elongation on placental size at term in Meishan pigs. *J. Anim. Sci.* 78:1047–1052.
- Wu, G., T. L. Ott, D. A. Knabe, and F. W. Bazer. 1999. Amino acid composition of the fetal pig. *J. Nutr.* 129:1031–1038.
- Youngs, C. R., L. K. Christenson, and S. P. Ford. 1994. Investigations into the control of litter size in swine: III. A reciprocal embryo transfer study of early conceptus development. *J. Anim. Sci.* 72:725–731.



**References**

This article cites 29 articles, 22 of which you can access for free at:  
<http://jas.fass.org/cgi/content/full/85/9/2093#BIBL>

**Citations**

This article has been cited by 1 HighWire-hosted articles:  
<http://jas.fass.org/cgi/content/full/85/9/2093#otherarticles>